Remarks

A. Pending Claims

Claims 1-32, 63 and 128 stand rejected. Claim 28 has been cancelled without prejudice. Claims 17, 22, 28 and 39 are presently amended. Claims 1-27, 29-32, 63 and 128 are pending in the case.

B. Changes to the Specification

Table 3 is presently amended to correct a typographical error appearing therein. The correction does not incorporate new matter.

C. Rejections Under 35 U.S.C.§103

Claims 1-19, 21, 23, 25, 27, 29, 30, 32, 63 and 128 stand rejected under to 35 U.S.C. §103(a) as being obvious over the teachings of U.S. Patent No. (USPN) 4,927,676 to Williams et al. (the '676 patent) in view of USPN 6,582,391 to Mineau-Hanschke (the '391 patent), and if necessary in view of USPN 5,034,265 to Hoffman et al. (the '265 patent) or USPN 6,033,582 to Lee et al. (the '582 patent) or USPN 5,055,316 to Hoffman et al. (the '316 patent).

Claims 1, 32, 63 and 128 have been amended to include the feature "wherein the living cells coupled to the treated substrate produce more of one or more cellular products than living cells coupled to an untreated substrate, and wherein at least one of the one or more cellular products is vascular endothelial growth factor (VEGF)." Support for the amendment may be found at least in paragraphs [0012], [0044], [0045], [0065] and [0075] and in the data set forth in Fig. 2 and Example 2 of the specification as filed. The prior art references, taken alone or in combination, appear to be silent on the combination of features set forth in the amended claims or any claims depending therefrom.

The combination of prior art references set forth above is further relied on to establish a *prima facie* case of obviousness of claims 20, 22, 24, 26, 28 and 31. For at least the same reasons set forth above, Applicant submits that the '676 patent, the '391 patent, the '265 patent, the '582 patent and the '316 patent, either alone or in combination, appear to be silent on the feature

"wherein the living cells coupled to the treated substrate produce more of one or more cellular products than living cells coupled to an untreated substrate, and wherein at least one of the one or more cellular products is vascular endothelial growth factor (VEGF)." Accordingly, Applicant submits that claims 20, 22, 24, 26, 28 and 31 are unobvious over the combined teachings thereof.

Regarding claim 28, the Office action states that USPN 6,419,920 to Mineau-Hanschke et al., (the '920 patent) "discloses vascular endothelial growth factor as a cellular product (col 4, lines 41-42). When using cells that produce a product as the cells of Williams et al as set forth above, it would have been obvious to use cells that produce vascular endothelial growth factor as suggested by Mineau-Hanschke." (Office action, page 6). Applicant respectfully disagrees with this statement.

The '920 patent appear to be silent on "cells that produce vascular endothelial growth factor." Instead, the '920 patent teaches that certain exogenous "agents" (which include various VEGF isoforms) can be added to the hybrid matrices disclosed therein. In this regard, the '920 patent states:

> "[H]ybrid matrices of the invention can also contain one or more (e.g., at least 2, 3, 4, 5, 6, 8, or 10) agents intended to improve the functioning of the matrix, e.g., by increasing proliferation and/or maintenance of the cells. These agents can include, for example, factors which promote vascularization, cytokines, or growth factors. While the agent used in a particular hybrid matrix and the polypeptide, e.g., a medically useful polypeptide, produced by the cells in the matrix can be the same substance, the two entities will generally be different. The agent can be added directly to the mixture used to make the hybrid matrices or can be bound to or encapsulated within a solid substrate which is added to the same mixture. ... Examples of agents which can be used in the matrices include basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), VEGF-A, VEGF-B, VEGF-C, VEGF-D, acidic fibroblast growth factor (aFGF), endothelial cell growth factor, platelet-derived growth factor (PDGF), endothelial cell stimulating angiogenesis factor (ESAF), leukotriene C_4, a prostaglandin, insulin-like growth factor 1 (IGF-1), granulocyte colony stimulating factor (G-CSF), angiogenin, transforming growth factor-α (TGF-α), transforming growth factor-β (TGF-β), ascorbic acid, epidermal growth factor (EGF), or oncostatin M. The bioactive concentration of each agent will vary greatly. A starting range is provided by the manufacturer and is usually based on a standard bioactivity assay using, for example, degree of cell proliferation as the end point." (The '920 patent, Col. 4, lines 4-55; *emphasis added*).

The '920 patent appears to be silent however, on VEGF expressed by cells present in the hybrid matrices. Instead, the '920 patent refers to such endogenously expressed factors as "medically useful polypeptides" (see Col. 2, line 55 – Col. 3, line22). The '920 patent does not

appear to teach that VEGF is among the "medically useful polypeptides" expressed by the cells. Instead, various isoforms of exogenously derived VEGF are added to the hybrid matrix during the manufacture thereof.

In light of the above, Applicant respectfully submits that claims 17 – 27, 29 – 30 and 39 are unobvious and patentable over the teachings of the '216 patent, and respectfully requests the withdrawal of the 35 USC §103 rejections.

D. Conclusion

Applicant submits that the claims are in condition for allowance. Favorable reconsideration is respectfully requested.

Applicant requests a 3-month extension of time for the submission of this paper. A fee authorization for the appropriate amount is filed herewith. If any additional fees are required, or have been overpaid, please appropriately charge or credit such fees to Meyertons, Hood, Kivlin, Kowert & Goetzel, P.C. Deposit Account Number 50-1505/5660-00503/EBM.

Respectfully submitted,

David W. Quimby
Reg. No. 39,338

Attorney for Applicant

MEYERTONS, HOOD, KIVLIN, KOWERT & GOETZEL, P.C.
P.O. BOX 398
AUSTIN, TX 78767-0398
(512) 853-8800 (voice)
(512) 853-8801 (facsimile)

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